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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/918,887	07/30/2001	Susanna M. Rybak	015280-325200US	5276

20350 7590 01/11/2005

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EXAMINER
SCHWADRON, RONALD B

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 01/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/918,887	RYBAK ET AL.	
	Examiner	Art Unit	
	Ron Schwadron, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,14-26* is/are pending in the application.

4a) Of the above claim(s) *15,12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,14,16-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. Applicant's election with traverse of antiCD22 and RFB4 in the reply filed on 7/16/2004 is acknowledged. The traversal is on the ground(s) that are stated. This is not found persuasive because the species are distinct for the reasons elaborated in the previous Office Action.

The requirement is still deemed proper and is therefore made FINAL.

2. Claim 12 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 7/16/2004.

3. Claims 1-11,14,16-26 are under consideration.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1,3,6-11,14,16,18,21-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 U.S.P.Q.2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the applicant had possession at the time of invention of the claimed invention.

The instant claims encompass an immunoconjugate that uses an onc protein in said immunoconjugate. The only onc protein disclosed in the specification is Onconase which comprises the particular amino acid sequences recited in claims 2,4,5. However, the claims under consideration would appear to encompass undisclosed alleles, variants and mutants of said protein that are not disclosed in the specification. The claims encompass a vast genus of immunoconjugates containing undisclosed onc proteins. In view of the aforementioned problems regarding description of the claimed invention, the specification does not provide an adequate written description of the invention claimed herein. See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1404-7 (Fed. Cir. 1997). In University of California v. Eli Lilly and Co., 39 U.S.P.Q.2d 1225 (Fed. Cir. 1995) the inventors claimed a genus of DNA species encoding insulin in different vertebrates or mammals, but had only described a single species of cDNA which encoded rat insulin. The court held that only the nucleic acids species described in the specification (i.e. nucleic acids encoding rat insulin) met the description requirement and that the inventors were not entitled to a claim encompassing a genus of nucleic acids encoding insulin from other vertebrates, mammals or humans, id. at 1240. In the instant case, the facts are similar to those disclosed in University of California v. Eli Lilly and Co. The Federal Circuit has held that if an inventor is "unable to envision the detailed constitution of a gene so as to distinguish it from other materials. . .conception has not been achieved until reduction to practice has occurred", Amgen, Inc. v. Chugai Pharmaceutical Co, Ltd., 18 U.S.P.Q.2d 1016 (Fed. Cir. 1991). Attention is also directed to the decision of The Regents of the University of California v. Eli Lilly and Company (CAFC, July 1997) wherein is stated: The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 222 USPQ 369, 372-373 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

Thus, as we have previously held, a cDNA is not defined or described by the mere name "cDNA," even if accompanied by the name of the protein that it encodes,

but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA. See Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606.

Regarding applicants comments, the instant claims encompass an immunoconjugate that uses an onc protein in said immunoconjugate. The only onc protein disclosed in the specification is Onconase which comprises the particular amino acid sequences recited in claims 2,4,5. However, the claims under consideration would appear to encompass undisclosed alleles, variants and mutants of said protein than are not disclosed in the specification. The claims encompass a vast genus of immunoconjugates containing undisclosed onc proteins. In view of the aforementioned problems regarding description of the claimed invention, the specification does not provide an adequate written description of the invention claimed herein. See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1404-7 (Fed. Cir. 1997). In University of California v. Eli Lilly and Co., 39 U.S.P.Q.2d 1225 (Fed. Cir. 1995) the inventors claimed a genus of DNA species encoding insulin in different vertebrates or mammals, but had only described a single species of cDNA which encoded rat insulin. The court held that only the nucleic acids species described in the specification (i.e. nucleic acids encoding rat insulin) met the description requirement and that the inventors were not entitled to a claim encompassing a genus of nucleic acids encoding insulin from other vertebrates, mammals or humans, id. at 1240.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 1,2,4-11,16,17,19,20,22-26 are rejected under 35 U.S.C. 102(e) as being anticipated by Goldenberg (US Patent 6,083,477).

Goldenberg teaches antiCD22 monoclonal antibody LL2 conjugated to the RNase EDN or Onconase in a pharmaceutical composition (such as tissue culture media) (see Example 2 in column 7, Example 8 in column 12 and Table 2). Onconase is an "onc protein". Furthermore, said Table 2 shows that the onc cytotoxic reagent attached to the LL2 antibody is at least 100 times more cytotoxic compared to the same antibody attached to EDN. The amino acid sequences recited in claims 2,4,5 are found in Onconase and therefore it is an inherent property of Onconase that it contains said amino acid sequences. Goldenberg teaches humanized LL2 and single chain monoclonal antibodies (see column 4, paragraphs 3 and 4).

Regarding the Goldenberg declaration filed 5/6/2003, whilst said declaration discloses that the subject matter referred to above was jointly invented by the inventors of the instant application, Goldenberg (US 6,653,104) claims essentially the same subject matter as disclosed above (see claims 1-8,11,12,19,21-23,24,26,27,30,32,33 92-98,101,102,112,113,114,116,122,123). The only "moiety having ribonucleolytic activity derived from a non-human ribonuclease" disclosed in Goldenberg (US 6,653,104) is Onconase. The functional property recited in claim 1 of the instant application appears to be present in any onconase/antiCD22 conjugate. Thus, the Goldenberg declaration filed 5/6/2003 is contradicted by the claims of Goldenberg (US 6,653,104) wherein Goldenberg is the sole inventor of the claimed subject matter.

8. Claims 1-9,14,16-25 are rejected under 35 U.S.C. 102(e) as being anticipated by Rybak et al. (US Patent 5,840,840).

Rybak et al. teach Onconase/antibody conjugates wherein the antibody binds a B cell marker (see column 11, second paragraph, column 8, first paragraph, abstract). Onconase is an "onc protein". The amino acid sequences recited in claims 2,4,5 are found in Onconase and therefore it is an inherent property of Onconase that it contains said amino acid sequences. Rybak et al. teach that the antibody can be a single chain antibody or humanized antibody wherein a humanized antibody is a monoclonal antibody (see column 8, last paragraph). Rybak et al. teach recombinant production of said conjugate wherein two components are joined (see column 9, last paragraph). The functional property of claim 1 is an inherent property of any Onconase/antibody conjugate. B cell idiotypes are present on B cell lymphomas. Rybak et al. teach pharmaceutical compositions of said conjugates (see column 11, fourth paragraph).

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 1-11,14,16-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goldenberg (US Patent 6,083,477) in view of Uhr et al. (US Patent 5,686,072). Goldenberg teaches antiCD22 monoclonal antibody LL2 conjugated to the RNase EDN or Onconase in a pharmaceutical composition (such as tissue culture media) (see Example 2 in column 7, Example 8 in column 12 and Table 2). Onconase is an "onc protein". Furthermore, said Table 2 shows that the onc cytotoxic reagent attached to the LL2 antibody is at least 100 times more cytotoxic compared to the same antibody attached to EDN. The amino acid sequences recited in claims 2,4,5 are found in Onconase. Goldenberg teaches humanized LL2 and single chain monoclonal antibodies (see column 4, paragraphs 3 and 4). Goldenberg does not teach use of RFB4 in said conjugate or that the conjugate is recombinantly made. Uhr et al. teach use of RFB4 in immunotoxins and the advantages of using said antibody in immunotoxins (see column 4, penultimate paragraph). The preparation of immunoconjugates using recombinant methods was known in the art (eg. see Example 3 in Goldenberg). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Goldenberg teaches the claimed invention except for use of RFB4 in said conjugate or that the conjugate is recombinantly made whilst Uhr et al. teach use of RFB4 in immunotoxins and the advantages of using said antibody in immunotoxins and the preparation of immunoconjugates using recombinant methods was known in the art. One of ordinary skill in the art would have been motivated to do the aformentioned because Uhr et al. teach use of RFB4 in immunotoxins and the advantages of using said antibody in immunotoxins and the advantages of preparation of proteins or fusion proteins using recombinant methods was known in the art.

Regarding the Rybak declaration filed 5/6/2003, said declaration does not address the invention addressed in this rejection (RFB4 Onconase conjugates).

11. Claims 1-11,14,16-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rybak (US Patent 5,840,840) in view of Uhr et al. (US Patent 5,686,072). Rybak et al. teach an Onconase/antibody conjugates wherein the antibody binds a B cell marker (see column 11, second paragraph, column 8, first paragraph, abstract). Onconase is an "onc protein". The amino acid sequences recited in claims 2,4,5 are found in Onconase. Rybak et al. teach that the antibody can be a single chain antibody or humanized antibody wherein a humanized antibody is a monoclonal antibody (see column 8, last paragraph). Rybak et al. teach recombinant production of said conjugate wherein two components are joined (see column 9, last paragraph). The functional property of claim 1 appears to be a property of any Onconase/antibody conjugate. Furthermore, since the claim does not specify how the EDN conjugate is made and the efficacy of said conjugate would depend on the method of conjugation, then any onc immunoconjugate would potentially be 100 times more cytotoxic than a EDN conjugate made using a method that produced an EDN conjugate with low activity. B cell idiotypes are present on B cell lymphomas. Rybak et al. teach pharmaceutical compositions of said conjugates (see column 11, fourth paragraph). Rybak et al. does not teach use of RFB4/antiCD22 antibody in said conjugate. Uhr et al. teach use of the antiCD22 antibody RFB4 in immunotoxins and the advantages of using said antibody in immunotoxins (see column 4, penultimate paragraph). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Rybak et al. teaches the claimed invention except for use of RFB4 in said conjugate whilst Uhr et al. teach use of RFB4 in immunotoxins and the advantages of using said antibody in immunotoxins. One of ordinary skill in the art would have been motivated to do the aformentioned because Uhr et al. teach use of RFB4 in immunotoxins and the advantages of using said antibody in immunotoxins and because Rybak et al. teach that their immunoconjugate can contain a recognition moiety which binds B cells (see column 11, second paragraph).

Regarding the Rybak declaration filed 5/6/2003, said declaration does not address the invention addressed in this rejection (RFB4 Onconase conjugates).

12. Claims 1-11,14,16-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Youle et al. (US Patent 6,649,393) in view of Uhr et al. (US Patent 5,686,072).

Youle et al. teach Onconase and recombinant immunoconjugates containing Onconase where the Onconase has the sequence or encompasses the sequence recited in the claims (see column 7, first two paragraphs, column 7, last paragraph, column 8, columns 11-12). Youle et al. teach that the antibody portion of the conjugate can be a Fv (column 11, third paragraph). Youle et al. teach that the antibody can be monoclonal (see column 12, second paragraphs). Humanized antibodies and the advantages of such antibodies were well known in the art. The functional property of claim 1 appears to be a property of any Onconase/antibody conjugate. Furthermore, since the claim does not specify how the EDN conjugate is made and the efficacy of said conjugate would depend on the method of conjugation, then any onc immunoconjugate would potentially be 100 times more cytotoxic than a EDN conjugate made using a method that produced an EDN conjugate with low activity. Youle et al. teach a pharmaceutical composition of said conjugate (see column 2, penultimate paragraph). Youle et al. does not teach use of RFB4/antiCD22 antibody in said conjugate. Uhr et al. teach use of the antiCD22 antibody RFB4 in immunotoxins and the advantages of using said antibody in immunotoxins (see column 4, penultimate paragraph). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Youle et al. teaches the claimed invention except for use of RFB4 in said conjugate whilst Uhr et al. teach use of RFB4 in immunotoxins and the advantages of using said antibody in immunotoxins. One of ordinary skill in the art would have been motivated to do the aformentioned because Uhr et al. teach use of RFB4 in immunotoxins and the advantages of using said antibody in immunotoxins and because Youle et al. teach that their immunoconjugate can be used to target cancer cells (see column 2, penultimate paragraph) whilst use of antiCD22/RFB4 to target B cell tumors was known in the art (see Uhr et al.).

Regarding the Rybak declaration filed 5/6/2003, said declaration does not address the invention addressed in this rejection (RFB4 Onconase conjugates).

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11

F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 1-11,14,16-26 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of U.S. Patent No. 6,653,104. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons. While the two sets of claims differ in scope Goldenberg (US 6,653,104) claims essentially the same subject matter as disclosed above (see claims 1-8,11,12,19,21-23,24,26,27,29,32,33,92-98,101,102,109,111,112,113,114,116,117,122,123). The only "moiety having ribonucleolytic activity derived from a non-human ribonuclease" disclosed in Goldenberg (US 6,653,104) is Onconase. The functional property recited in claim 1 of the instant application appears to be present in any onconase/antiCD22 conjugate.

15. The previously pending rejection of claim 14 under 35 USC 112 second paragraph as per page 3 of the Office Action mailed 1/28/2003 is withdrawn in view of applicants arguments.

16. The previously pending rejection of claims 1,3,6-12,14,16,18,21-26 under 35 USC 112 first paragraph as lacking enablement for the reasons as per pages 4-5 of the Office Action mailed 1/28/2003 is withdrawn in view of applicants arguments.

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ron Schwadron, Ph.D. whose telephone number is 571 272-0851. The examiner can normally be reached on Monday-Thursday 7:30-6:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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